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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/085,117	02/27/2002	David W. Morris	529452000121	7176
55255	7590	08/28/2006	EXAMINER	
SAGRES DISCOVERY INC. INTELLECTUAL PROPERTY - R440 P.O. BOX 8097 EMERYVILLE, CA 94662-8097				AEDER, SEAN E
ART UNIT		PAPER NUMBER		
		1642		

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/085,117	MORRIS ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Sean E. Aeder, Ph.D.	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 20 March 2006.

2a)  This action is FINAL.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4)  Claim(s) 20-31 is/are pending in the application.  
4a) Of the above claim(s) 22 is/are withdrawn from consideration.  
5)  Claim(s) \_\_\_\_\_ is/are allowed.  
6)  Claim(s) 20,21 and 23-31 is/are rejected.  
7)  Claim(s) \_\_\_\_\_ is/are objected to.  
8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)  The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3)  Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
    Paper No(s)/Mail Date .  
4)  Interview Summary (PTO-413)  
    Paper No(s)/Mail Date. \_\_\_\_ .  
5)  Notice of Informal Patent Application (PTO-152)  
6)  Other: sequence comparison.

***Detailed Action***

The Election filed 3/20/06 in response to the Office Action of 6/1/05 is acknowledged and has been entered. Applicant elected group VI and human EGR1 (SEQ ID NO:167) with traverse.

The traversal is on the ground(s) that a search and examination of more than one group would not impose a serious burden on the examiner. Applicant asserts that searching group III (a method of screening drug candidates) together with elected group VI (a method of diagnosing carcinoma or a propensity of carcinoma) would not constitute a serious burden. Applicant argues that the same field of search is appropriate for group III and group VI. Applicant further argues that a search of elected SEQ ID NO:167 would provide results relevant to both group VI and unelected group III. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of groups III and VI are distinct for the reasons set forth in the Office Action. Each group comprises distinct steps, utilizes different products, and differs at least in objectives and criteria for success, which demonstrates that each method has a different mode of operation. Searching and examining both of these methods would result in a serious burden on the examiner. Furthermore, it is noted that the literature search, particularly relevant in this art, is not coextensive and is very important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-19 were pending.

Claims 1-19 were cancelled by Applicant.

Claims 20-31 were newly added by Applicant.

Claim 22 is withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 20, 21, and 23-31 are currently under consideration.

### ***Claim Objections***

Claims 20, 21, and 23-31 are objected to for encompassing unelected inventions.

Claims 20, 21, and 23-31 encompass unelected cancer associated (CA) genes and their respective SEQ ID NOs. Further, it is noted that the SEQ ID NO:167 represents the elected invention and is not a species. Proper correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20, 21, and 24-31 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 and dependent claim 21 are rejected because claim 20 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. Claim 20 recites a method of detecting cancer wherein detecting some kind of differential expression of a CA gene is indicative of cancer; however, it is unclear what expression of a gene in a patient sample is compared in order to determine a differential expression. Further, it is unclear what kind of differential expression would be indicative of cancer. For example, the claims do not recite whether an increase or a decrease in expression, as compared to some kind of control, is indicative of cancer. Thus, there are missing steps involving comparing and correlating. See MPEP § 2172.01.

Claims 24, 27, and dependent claims 25, 26, and 28-31 are rejected because claims 24 and 27 recite: "...an unaffected individual...". It is unclear what Applicant means by "unaffected". It is unclear what would not have affected said unaffected individual.

Claim 24 and dependant claims 25-26 are rejected because claim 24 recites: "...a decrease of at least 50% between the level of mRNA in (a) and the level of mRNA in the second or the third sample ...". It is unclear from which sample a decrease in expression would be indicative of cancer or a predisposition to cancer. Further, it is unclear from which sample a measurement is calculated in order to determine how much expression constitutes a 50% decrease. Given the above reasons, the metes and bounds of the claims cannot be determined.

Claim 27 and dependant claims 28-31 are rejected because claim 27 recites: "...a decrease of at least about 50% between the level of CA gene expression in (a) and the level of CA gene expression in the second or the third sample ...". It is unclear from which sample a decrease in expression would be indicative of cancer or a predisposition to cancer. Further, it is unclear from which sample a measurement is calculated in order to determine how much expression constitutes a 50% decrease. Given the above reasons, the metes and bounds of the claims cannot be determined.

Claim 29 is rejected for reciting: "...wherein the decrease between the level of CA gene expression in (a) and the level of the CA gene expression in the second or third sample ...". It is unclear from which sample a decrease in expression would be indicative of cancer or a predisposition to cancer. Further, it is unclear from which sample a measurement is calculated in order to determine how much expression constitutes a 100% decrease. Given the above reasons, the metes and bounds of the claims cannot be determined.

Claim 24 recites the limitation "the level of mRNA in (a)". There is insufficient antecedent basis for this limitation in the claim. It is unclear whether "the level of mRNA in (a)" means the level of total mRNA in a first sample, the level of mRNA of a specific (CA) gene having the nucleic acid sequence of SEQ ID NO:167 in said first sample, or

something else. Given the above reasons, the metes and bounds of the claims cannot be determined.

Claim 24 recites the limitation "a level of the mRNA in a second sample". There is insufficient antecedent basis for this limitation in the claim. It is unclear whether "a level of the mRNA in a second sample" means the level of total mRNA in said second sample, the level of mRNA of a specific (CA) gene having the nucleic acid sequence of SEQ ID NO:167 in said second sample, or something else. Given the above reasons, the metes and bounds of the claims cannot be determined.

Claim 24 recites the limitation "a level of the mRNA in a third sample". There is insufficient antecedent basis for this limitation in the claim. It is unclear whether "a level of the mRNA in a third sample" means the level of total mRNA in said third sample, the level of mRNA of a specific (CA) gene having the nucleic acid sequence of SEQ ID NO:167 in said third sample, or something else. Given the above reasons, the metes and bounds of the claims cannot be determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20, 21, and 23-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for diagnosing prostate cancer

comprising detecting an increase in Egr-1 gene expression (SEQ ID NO:167) in a prostate tissue sample as compared to Egr-1 gene expression (SEQ ID NO:167) in a normal prostate tissue, does not reasonably provide enablement for a method of diagnosing every other type of cancer comprising detecting just any type of change in expression of just any CA gene in just any type of sample, as compared to any type of control. Further, the specification does not enable any kind of diagnostic assay wherein one would be able to predictably determine whether someone has a predisposition to any cancer by measuring expression of Egr-1 (SEQ ID NO:167) in any sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The instant claims are broadly drawn to a method of diagnosing every type of cancer and methods of determining whether a person has a predisposition for every type of cancer comprising detecting just any type of change in just any CA gene in just any type of sample, as compared to any type of control.

The specification discloses that SEQ ID NO:167 is a cancer associated (CA) nucleic acid (page 10 lines 9-12 and table 29, in particular). The specification further discloses that CA nucleic acids are nucleic acids that were identified through use of oncogenic retroviruses, whose sequences insert into the genome of lymphatic tissue resulting in carcinoma (page 3 lines 17-29 and page 7 lines 20-24, in particular). Further, the specification prophetically states that “oncogenes that are identified in one type of cancer such as lymphoma or leukemia have a strong likelihood of being involved in other types of cancers as well...” (page 3 lines 21-24).

The specification lacks any working example showing that SEQ ID NO:167 is aberrantly expressed in any cancer type. Further, undue experimentation would be required to determine whether the expression level of SEQ ID NO:167 is indicative of every carcinoma or indicative of a predisposition for every cancer. However, the teachings of Eid et al (Cancer Research, 6/1/98, 58:2461-2468) demonstrate that an increase in Egr-1 expression in prostate biopsies from a subject, as compared to Egr-1 expression in normal prostate tissue, is indicative that said subject has prostate cancer (Figure 2, in particular). The prior art does not teach or suggest that methods of measuring Egr-1 (SEQ ID NO:167) expression could be used to determine whether a patient has a predisposition to any kind of tumor with any predictability of success.

The state of the prior art dictates that if a molecule such as a specific polynucleotide, such as that set forth in SEQ ID NO:167, is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed

polynucleotide to be used in a diagnostic manner. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful clinical application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence of the polynucleotide's expression including the correlation to a diseased state, one of

skill in the art would not be able to predictably use the polynucleotides in any diagnostic setting without undue experimentation.

The level of unpredictability for the detection of any disease and the detection of a predisposition to any disease is quite high. Since neither the specification nor the prior art provide evidence of a universal association between the claimed method and every cancer and every type of sample, a practitioner wishing to practice the claimed invention would be required to provide extensive experimentation to demonstrate such an association. Such experimentation would in itself be inventive.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to a method of diagnosing and determining whether a person has just any type of cancer or has a predisposition for just any type of cancer comprising detecting just any type of change expression in just any CA gene in just any type of sample, as compared to any type of control, and Applicant has not enabled said methods because it has not been shown that detecting every type of differential expression of every type of CA gene, as compared to every type of control, in every type of sample, could predictably be used as a universal method to determine whether a person has just any type of cancer or is predisposed to having any type of cancer.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as broadly claimed.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 21, 24-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Eid et al (Cancer Research 58, 2461-2468) as evidenced by Monia et al (US Patent 6,008,048; 12/28/99).

Claim 20 is drawn to a method of diagnosing cancer in a patient comprising detecting the presence of differential expression of a polynucleotide that has the nucleotide sequence set forth in SEQ ID NO:167 in a patient sample, wherein the presence of differential expression of the nucleotide sequence set forth in SEQ ID NO:167 in said sample is indicative of a patient who has cancer. Claim 21 is drawn to the method of claim 20 wherein the cancer is prostate cancer. Claim 24 is drawn to a method of diagnosing cancer comprising (a) measuring a level of mRNA of a polynucleotide that has the nucleotide sequence set forth in SEQ ID NO:167 in a first sample, said first sample comprising a first tissue type of a first individual, and (b) comparing the level of mRNA in (a) to (1) a level of mRNA in a second sample, said second sample comprising a normal tissue type of said first individual, or (2) a level of the mRNA in a third sample, said third sample comprising a normal tissue type from an unaffected individual, wherein a decrease of at least 50% between the level of mRNA in

(a) and the level of the mRNA in the second sample or the third sample indicates that the first individual has cancer. Claim 25 is drawn to method of claim 25 wherein the mRNA has the nucleotide sequence of SEQ ID NO:167. Claim 26 is drawn to the method of claim 24, wherein the cancer is prostate. Claim 27 is drawn to a method of diagnosing cancer comprising (a) measuring a level of the nucleotide sequence set forth in SEQ ID NO:167 in a first sample, said first sample comprising a first tissue type of a first individual and (b) comparing the level of expression of the nucleotide sequence set forth in SEQ ID NO:167 in (a) to (1) a level of expression of the nucleotide sequence set forth in SEQ ID NO:167 in a second sample, said second sample comprising a normal tissue type of said first individual or (2) a level of expression of the nucleotide sequence set forth in SEQ ID NO:167 in a third sample, said third sample comprising a normal tissue type from an unaffected individual, wherein a decrease of at least about 50% between the level of expression of the nucleotide sequence set forth in SEQ ID NO:167 in (a) and the level of expression of the nucleotide sequence set forth in SEQ ID NO:167 in the second sample or third sample indicates that the first individual has cancer. Claim 28 is drawn to the method of claim 27 wherein the cancer is prostate cancer. Claim 29 is drawn to the method of claim 24 or 27 wherein the decrease between the level of expression of the nucleotide sequence set forth in SEQ ID NO:167 in (a) and the level of expression of the nucleotide sequence set forth in SEQ ID NO:167 in the second sample or the third sample is 100%. Claim 30 is drawn to the method of claim 27, wherein the level of expression of the nucleotide sequence set forth

in SEQ ID NO:167 is determined by measuring mRNA levels. Claim 31 is drawn to the method of claim 30 wherein the mRNA has the sequence of SEQ ID NO:167.

Eid et al teaches a method of diagnosing prostate cancer in a patient comprising detecting the presence of differential expression of Egr-1 in a patient sample, wherein the presence of differential expression of Egr-1 in said sample, as compared to Egr-1 expression in a control sample, indicates a patient has prostate cancer (Figure 2, in particular). As evidenced by Monia et al, SEQ ID NO:167 is Egr-1 (see attached sequence comparison of SEQ ID NO:47 taught by Monia et al and instant SEQ ID NO:167, in particular). Eid et al further teaches that “normal” control samples are prostate tissues from autopsies of young organ donors and non-malignant prostate tissues from patients that underwent a prostatectomy (page 2461 right column, in particular). Eid et al further teaches a method wherein a decrease of at least 50% between the level of Egr-1 mRNA in a first sample, said first sample comprising a first tissue type of a first individual, and the level of Egr-1 mRNA in said control samples indicates that said first sample was obtained from a patient with prostate cancer (see Figure 2, in particular). Eid et al further teaches a decrease of 100% between the level of Egr-1 mRNA in said first sample and the level of the Egr-1 mRNA in said control samples.

### ***Summary***

No claim is allowed. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, but free of the prior art teaching a method of diagnosing cancer comprising detecting

the presence of differential expression of a gene having the polynucleotide sequence of SEQ ID NO:167 in a patient sample, wherein downregulation of the polynucleotide having the sequence of SEQ ID NO:167 in a patient sample, as compared to a control, is indicative of cancer. The closest prior art for claim 23 is Eid et al (Cancer Research 58, 2461-2468), which teaches a method of diagnosing cancer comprising detecting the presence of differential expression of a gene having the polynucleotide sequence of SEQ ID NO:167 in a patient sample, wherein *upregulation* of the polynucleotide having the sequence of SEQ ID NO:167 in a patient sample, as compared to a control, is indicative of cancer; however, this reference does not teach or suggest a method of diagnosing cancer comprising detecting the presence of differential expression of a gene having the polynucleotide sequence of SEQ ID NO:167 in a patient sample, wherein *downregulation* of the polynucleotide having the sequence of SEQ ID NO:167 in a patient sample, as compared to a control, is indicative of cancer.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA



JEFFREY SIEW  
SUPERVISORY PATENT EXAMINER

Db 3001 TTGTACTTGTGTTGGCTAACAAAGTGAATGGTGTGGCTATAAACACATTGAATGGCT 3060  
 Qy 3061 TTATTGCCATGGGATATGGTGTATATCCTTCCAAAAAATTAACGAAATAAGTA 3120  
 Db 3061 TTATTGCCATGGGATATGGTGTATATCCTTCCAAAAAATTAACGAAATAAGTA 3120  
 Qy 3121 GCTGCGATGGG 3132  
 Db 3121 GCTGCGATGGG 3132  
 Qy 601 AACAAAGGAAAGGTGGCTGGAGAACCCAGTTACCCAGCAAAACCTGACTGCC 660  
 Db 601 AACAAAGGAAAGGTGGCTGGAGAACCCAGTTACCCAGCAAAACCTGACTGCC 660  
 Qy 661 ATCACCTATACTGGCCCTTCCCTGGAGCCACCCAGTGGCAACACCTTGTGG 720  
 Db 661 ATCACCTATACTGGCCCTTCCCTGGAGCCACAGTGGCAACACCTTGTGG 720  
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 Db 721 CCGAGGCCCCCTCTTCAGCTTGCTAGTGGCTTGTAGCCAAACCCACGGCCTCC 780  
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 Db 781 TCGTCCTCAGCACCATCTCCAGGGGCTCTCGCCTCCAGGGCCACCCCTG 840  
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 Db 841 AGCTGGCGAGTGCATCCACAGGACGAGTCCATTTACTCAAGGGCACCCACCTTCCCC 900  
 Qy 901 ACGCCGAAACTGGAATTTCCCTAGCCAAAGCCAGGCTTCCAGGGGACCTTCCCC 960  
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RESULT 3  
 US-09-300-958A-32  
 ; Sequence 32, Application US/09300958A  
 ; Patent No. 6495319  
 ; GENERAL INFORMATION:  
 ; APPLICANT: McClelland, Michael  
 ; APPLICANT: Welsh, John  
 ; APPLICANT: Trenkle, Thomas  
 ; TITLE OF INVENTION: Reduced Complexity Nucleic Acid Targets and Methods of  
 ; TITLE OF INVENTION: Using Same  
 ; FILE REFERENCE: P-PH 3457  
 ; CURRENT APPLICATION NUMBER: US/09/300,958A  
 ; CURRENT FILING DATE: 1999-04-27  
 ; PRIOR APPLICATION NUMBER: 60/083,331  
 ; PRIOR FILING DATE: 1998-04-27  
 ; PRIOR APPLICATION NUMBER: 60/098,070  
 ; PRIOR FILING DATE: 1998-08-27  
 ; PRIOR APPLICATION NUMBER: 60/118,624  
 ; PRIOR FILING DATE: 1999-02-04  
 ; NUMBER OF SEQ ID NOS: 85  
 ; SOFTWARE: PatentIn Ver. 2.0  
 ; SEQ ID NO: 32  
 ; LENGTH: 3132  
 ; TYPE: DNA  
 ; ORGANISM: Homo sapiens  
 US-09-300-958A-32

Query Match 100.0%; Score 3132; DB 3; Length 3132;  
 Best Local Similarity 100.0%; Pred. No. 0;  
 Matches 3132; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	Db	Score	Length
1 CCGCAGAACTTGGGAGCCGCCGCGCTTCCGGCCGGCGCCAGGCCAAGGGCTTCCGGCCGGCA	1 CCGCAGAACTTGGGAGCCGCCGCGCTTCCGGCCGGCGCCAGGCCAAGGGCTTCCGGCCGGCA	60	60
61 GGACCGGCCCCCTGCCAGGCTCGCCGCCGCTTCCGGCCGGCGCCAGGCCAAGGGCTTCCGGCCGGCA	61 GGACCGGCCCCCTGCCAGGCTCGCCGCCGCTTCCGGCCGGCGCCAGGCCAAGGGCTTCCGGCCGGCA	120	120
61 GGACGGGCCCCCTGCCAGGCTCGCCGCCGCTTCCGGCCGGCGCCAGGCCAAGGGCTTCCGGCCGGCA	61 GGACGGGCCCCCTGCCAGGCTCGCCGCCGCTTCCGGCCGGCGCCAGGCCAAGGGCTTCCGGCCGGCA	120	120
121 CGGAGTCTGGGTGCGCGCTGAGCTTCTCAAGTGTTCCTCCGGCCATGTAACCCG	121 CGGAGTCTGGGTGCGCGCTGAGCTTCTCAAGTGTTCCTCCGGCCATGTAACCCG	180	180
121 CGGAGTCTGGGTGCGCGCTGAGCTTCTCAAGTGTTCCTCCGGCCATGTAACCCG	121 CGGAGTCTGGGTGCGCGCTGAGCTTCTCAAGTGTTCCTCCGGCCATGTAACCCG	180	180
181 GCCAGGGCCCCGCAACGCTTCCCTGCGAGCTTCCGGCCGGCGCCAGGCCAAGGGCTTCCGGCCGGCA	181 GCCAGGGCCCCGCAACGCTTCCCTGCGAGCTTCCGGCCGGCGCCAGGCCAAGGGCTTCCGGCCGGCA	240	240
181 GCCAGGGCCCCGCAACGCTTCCCTGCGAGCTTCCGGCCGGCGCCAGGCCAAGGGCTTCCGGCCGGCA	181 GCCAGGGCCCCGCAACGCTTCCCTGCGAGCTTCCGGCCGGCGCCAGGCCAAGGGCTTCCGGCCGGCA	240	240
241 GACACCAAGCTTCCAGGATGGCTGGCGGGCAAGGGCCAGATGCACTGGCT 300	241 GACACCAAGCTTCCAGGATGGCTGGCGGGCAAGGGCCAGATGCACTGGCT 300	300	300
241 GACACCAAGCTTCCAGGATGGCTGGCGGGCAAGGGCCAGATGCACTGGCT 300	241 GACACCAAGCTTCCAGGATGGCTGGCGGGCAAGGGCCAGATGCACTGGCT 300	420	420
301 ATGTCCTGGCTGCGATCTCTGACCCGTTCCGGATCTTCCCTCACTGGCCACATGGAC 360	301 ATGTCCTGGCTGCGATCTCTGACCCGTTCCGGATCTTCCCTCACTGGCCACATGGAC 360	360	360
361 AACTACCCTAAGCTGGAGGAGATGATGCTGCTGAGCAACGGGCTCCAGTCTGGC 420	361 AACTACCCTAAGCTGGAGGAGATGATGCTGCTGAGCAACGGGCTCCAGTCTGGC 420	420	420
361 AACTACCCTAAGCTGGAGGAGATGATGCTGCTGAGCAACGGGCTCCAGTCTGGC 420	361 AACTACCCTAAGCTGGAGGAGATGATGCTGCTGAGCAACGGGCTCCAGTCTGGC 420	480	480
421 GCCGGGGGGCCCCAGAGGGAGGGAGGGAGGGCTGCTGAGCAACGGGAGGGGGGGGT 480	421 GCCGGGGGGCCCCAGAGGGAGGGAGGGAGGGCTGCTGAGCAACGGGAGGGGGGGGT 480	480	480

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Qy	841	AGCTGGCGAGTGCATCCAACGACAGTCCATTAACTCAGGGCACCCATTAACTCAGGGCACCCATTCCC	900	Qy	1921	GGAAAAAGGGAGAAACAAACAGAGACTTAAGGACAGGAGGAGATGGCCATA	1980
Db	841	AGCTGGCGAGTGCATCCAACGACAGTCCATTAACTCAGGGCACCCATTCCC	900	Db	1921	GGAAAAAGGGAGAAACAAACAGAGACTTAAGGACAGGAGGAGATGGCCATA	1980
Qy	901	ACGGCGAACACTGACATTTCCTGAGCCAAGGCCAGGCCATTACTCAGGGCACCCATTCCC	960	Qy	1981	GGAGGAGGGGTTCCCTTAAGGTCAAGTGGAGGTCTACAGGCCAACTCCCTCTCTA	2040
Db	901	ACGGCGAACACTGACATTTCCTGAGCCAAGGCCAGGCCATTACTCAGGGCACCCATTCCC	960	Db	1981	GGAGGAGGGGTTCCCTTAAGGTCAAGTGGAGGTCTACAGGCCAACTCCCTCTCTA	2040
Qy	961	ACAGGGCTCCAGTACCCGCCATTACCTGCCAGGTTCCAGGTTCCC	1020	Qy	2041	CTGGAGTGGAGGTCTATGGCCAAACATCCCTCTGCCAATTAC	2100
Db	961	ACAGGGCTCCAGTACCCGCCATTACCTGCCAGGTTCCAGGTTCCC	1020	Db	2041	CTGGAGTGGAGGTCTATGGCCAAACATCCCTCTGCCAATTAC	2100
Qy	1021	ATGATCCCGACTACCTGTTCCACAGCGAGGGGATCTGGGCTGGCCACCCAGAC	1080	Qy	2101	TATCCCTTGAGCTCAGTGCCTGAAACAGCCATGTCCAAAGTCTATCCAA	2160
Db	1021	ATGATCCCGACTACCTGTTCCACCTGCCCTACCTGCCAGGTTCCC	1080	Db	2101	TATCCCTTGAGCTCAGTGCCTGAAACAGCCATGTCCAAAGTCTATCCAA	2160
Qy	1081	CAGAAGCCCTCCAGGGCCTGGAGGCCAGCCAGGCTTCGTAACCCCTCTGCT	1140	Qy	2161	AGAACTTGATTTGCAATGGATAAATCAATTCACTGATCATCTCCATATGCCT	2220
Db	1081	CAGAAGCCCTCCAGGGCCTGGAGGCCAGCCAGGCTTCGTAACCCCTCTGCT	1140	Db	2161	AGAACTTGATTTGCAATGGATAAATCAATTCACTGATCATCTCCATATGCCT	2220
Qy	1141	ACTATTAGGGCTTGGCACTCAGTCCGGGCTCCAGGAGCTGAAGGCCCTCATACAGC	1200	Qy	2221	GACCCCTTGGCCCTGACCCCTTGACAGTGTCTGCCATGGATTGGGGCTC	2280
Db	1141	ACTATTAGGGCTTGGCACTCAGTCCGGGCTCCAGGAGCTGAAGGCCCTCATACAGC	1200	Db	2221	GACCCCTTGGCCCTGACCCCTTGACAGTGTCTGCCATGGATTGGGGCTC	2280
Qy	1201	TACCACTCCAGCTCATCAACCCAGGGGCAATGCGCAAGTATCCCACCGGCAAG	1260	Qy	2281	AGAGCCCTTGGCCCTGACCCCTTGACAGTGTCTGCCATGGATTGGGGT	2340
Db	1201	TACCACTCCAGCTCATCAACCCAGGGGCAATGCGCAAGTATCCCACCGGCAAG	1260	Db	2281	AGAGCCCTTGGCCCTGACCCCTTGACAGTGTCTGCCATGGATTGGGGT	2340
Qy	1261	AGGCCCCCCACGAACGCCCTTAACGGCAACGCCATTACGGGATCTCTCC	1320	Qy	2341	ACTCTTGATGTGAAGATAATTGGCATATTCTATGGATTGGGATTTGGGGTTAGGTCTCACT	2400
Db	1261	AGGCCCCCCACGAACGCCCTTAACGGCAACGCCATTACGGGATCTCTCC	1320	Db	2341	ACTCTTGATGTGAAGATAATTGGCATATTCTATGGATTGGGATTTGGGGTTAGGTCTCACT	2400
Qy	1321	CGCTCCGAGGGCTCACCCGCCACATCCGGATCCACACGGCCAGGCCCTCCAGTGC	1380	Qy	2401	TGGGGGAAAGGGGAAAGGGCAACCAATGGTGAATCTCTATTTGGATGTA	2460
Db	1321	CGCTCCGAGGGCTCACCCGCCACATCCGGATCCACACGGCCAGGCCCTCCAGTGC	1380	Db	2401	TGGGGGAAAGGGGAAAGGGCAACCAATGGTGAATCTCTATTTGGATGTA	2460
Qy	1381	CGCATCTGGCATGGCAACTTCAGGCCAGGCCACCTACCCACATCCGGCACCCAC	1440	Qy	2461	TGCTGTGACATAAGTTGGTAAACCTTTGGAAACAGCAGTCTCAGAGC	2520
Db	1381	CGCATCTGGCATGGCAACTTCAGGCCAGGCCACCTACCCACATCCGGCACCCAC	1440	Db	2461	TGCTGTGACATAAGTTGGTAAACCTTTGGAAACAGCAGTCTCAGAGC	2520
Qy	1441	ACAGGGAAAGCCCTTCGGCTGGACATCTGTGGAAAGGAAAGTTGGCAGGAGGATGAA	1500	Qy	2521	ATGTTGGCAAAATAATGGTTGGTAAACTGCTTGGCTGACTCTCACA	2580
Db	1441	ACAGGGAAAGCCCTTCGGCTGGACATCTGTGGAAAGGAAAGTTGGCAGGAGGATGAA	1500	Db	2521	ATGTTGGCAAAATAATGGTTGGTAAACTGCTTGGCTGACTCTCACA	2580
Qy	1501	CGCAAGAGGCATACCAAGATCCACTTGGCGAGAAGGCAAGAACAGTGT	1560	Qy	2581	TGTTGGCAAAATAAGGGAGGCTTGGGAGCAAAATAAGGAAGAGGGCTGAGCTGAGCTTCTCC	2640
Db	1501	CGCAAGAGGCATACCAAGATCCACTTGGCGAGAAGGCAAGAACAGTGT	1560	Db	2581	TGTTGGCAAAATAATGGTTGGTAAACTGCTTGGCTGACTCTCACA	2640
Qy	1561	GTGGCCTCTGGCCACCCCTCTCTTACCCGTACTCTTACCTCCCTGCTACTCTTAC	1620	Qy	2641	TTTGGTTAAAGAGTTCACTGCTTGGCTTGGCTGATGCCCTTGCTGATGGCTT	2700
Db	1561	GTGGCCTCTGGCCACCCCTCTCTTACCCGTACTCTTACCTCCCTGCTACTCTTAC	1620	Db	2641	TTTGGTTAAAGAGTTCACTGCTTGGCTGATGCCCTTGCTGATGGCTT	2700
Qy	1621	CGTCCCCGGTTACTACCTCTTACCCGGCCACACCTCATACCCCTGCTACTCTG	1680	Qy	2701	GACATGTGCAATTGGGAGGACATGGTCACTGCTTGGCTGATGCCCTTGCTGATGGCTT	2760
Db	1621	CGTCCCCGGTTACTACCTCTTACCCGGCCACACCTCATACCCCTGCTACTCTG	1680	Db	2701	GACATGTGCAATTGGGAGGACATGGTCACTGCTTGGCTGATGCCCTTGCTGATGGCTT	2760
Qy	1681	CCACACCTCCCTCCCTCCGGCTCAGACCTACCCATCCCTGCTACTCTG	1740	Qy	2761	ATTGGGGAGGCTTGGGAGCAAAATAAGGAAGAGGGCTGAGCTGAGCTTCTCC	2820
Db	1681	CCACACCTCCCTCCCTCCGGCTCAGACCTACCCATCCCTGCTACTCTG	1740	Db	2761	ATTGGGGAGGCTTGGGAGCAAAATAAGGAAGAGGGCTGAGCTGAGCTTCTCC	2820
Qy	1741	CCCTCCCCGGTGGGGCACCCAGCTGACTCTCCCTCCGGCCACCAAGGTG	1800	Qy	2821	AGAATGTAAGAAAACAAATCTAAACAAATACTGAAACTCTAAAGTTTAA	2880
Db	1741	CCCTCCCCGGTGGGGCACCCAGCTGACTCTCCCTCCGGCCACCAAGGTG	1800	Db	2821	AGAATGTAAGAAAACAAATCTAAACAAATACTGAAACTCTAAAGTTTAA	2880
Qy	1801	AGCAGCTCCCTCCCTCAGCTGACCAACTCCCTCAGGCCCTCCAGGGCTTCGGAC	1860	Qy	2881	CTGAAAATGTAAGAAAACAAATCTAAACAAATACTGAAACTCTAAAGTTTAA	2940
Db	1801	AGCAGCTCCCTCCCTCAGCTGACCAACTCCCTCAGGCCCTCCAGGGCTTCGGAC	1860	Db	2881	CTGAAAATGTAAGAAAACAAATCTAAACAAATACTGAAACTCTAAAGTTTAA	2940
Qy	1861	ATGACAGCAACCTTTCTCCAGGACAATTGAAATTGCTAAAGGAAAGGAAAGAA	1920	Qy	2941	AGGGGGGATTTCTCCAGGACAATTGCTAAAGGAAAGGAAAGGAAAGAA	3000
Db	1861	ATGACAGCAACCTTTCTCCAGGACAATTGCTAAAGGAAAGGAAAGGAAAGAA	1920	Db	2941	AGGGGGGATTTCTCCAGGACAATTGCTAAAGGAAAGGAAAGGAAAGAA	3000
Qy	1861	ATGACAGCAACCTTTCTCCAGGACAATTGCTAAAGGAAAGGAAAGGAAAGAA	1920	Qy	3001	TTGTACTTGTGTTGGCTAAACAAAGTGACTGTTGGCTATAAACACATGAAATGGGCT	3060